

REMARKS

I. Status of the Claims

Claims 1-23, 28, 29, and 39-44 are pending in this application. Claims 3, 9, and 41-44 have been withdrawn from consideration. Claims 1, 2, 4-8, 10-23, 28, 29, 39, and 40 stand rejected. Claims 1, 22, 23, 28, and 29 have been amended to recite that plasticizer in the composition is "from 0.05 percent by weight to 2.5 percent by weight." Support for the amendments to these claims can be found, for example, in the specification at the last full paragraph of page 13 (ll. 22-27) and at pages 15-17 (Examples 1-5). Claim 23 has also been amended to recite a process for "the treatment of androgenic alopecia, comprising applying to a patient in need or desire thereof a composition comprising: . . ." Support for this amendment can be found, for example, in the specification at 4, ll. 7-21. Thus, no new matter has been introduced by the amendments to the claims.

II. Rejections Under 35 U.S.C. § 103(a)

A. Claims 1, 2, 4-8, 11-14, 22, 23, 28, 29 and 40

Claims 1, 2, 4-8, 22, 23, 28, 29 and 40 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 4,946,870 ("*Gaillard*"), in view of U.S. Patent No. 4,946,870 ("*Partain*"), US Patent No. 5,658,559 ("*Smith*"), and the August 1997 Cremophor® RH 40 Technical Information ("Cremophor® pamphlet"). Office Action at 2. According to the Office, "[t]he rejection is maintained for the reasons of record." *Id.* Applicants respectfully traverse the rejection for the reasons of record and the additional following arguments.

1. **Showing that there would have been a reasonable expectation of success after combining the cited references is a requirement of an obviousness rejection**

The Office also responds to Applicants' arguments presented in the Reply to the Office Action dated April 4, 2008. *Id.* at 2-5. In particular, the Office addresses Applicants' argument that the cited art cannot be used to establish a *prima facie* case of obviousness, because it fails to teach or suggest the inclusion of a plasticizer in the claimed composition. *Id.* at 3. Relying on *Ex parte Obiaya*, the Office alleges that:

In this case, regardless of whether POE hydrogenated castor oil is employed as a plasticizer or solvent, the very same component exerts the same benefits to the composition. The 'suppleness and flexibility' that is observed from the present invention would also [be] present [in] a composition which employs POE hydrogenated castor oil [in] which [it] is employed as a solvent.

Id. at 3.

With regard to Applicants' argument that an ordinarily skilled artisan would have been unable to reasonably anticipate the success of the claimed invention, the Office states that the rejection "is not based on an 'obvious to try' rationale." *Id.* at 4. Rather than explaining why one of ordinary skill would have had a reasonable expectation of success, the Office simply stated that: "[a] *prima facie* case of obviousness has been established because the references provide sufficient motivation to combine the components for their specific known benefits to make a topical anti-alopecia and/or acne composition in similar type of vehicles, i.e., lotion." *Id.* at 4. That is the Office seems to believe a *prima facie* case of obviousness only requires a showing that one of skill in the art would have combined the references, and that showing reasonable expectation of success is not necessary. However, such is not the proper standard.

Applicants respectfully remind the Office that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art" at the time the invention was made. M.P.E.P. § 2143.01(III), internal citation omitted, emphasis in original. Applicants respectfully point out that the Office has failed to articulate any reason why one of ordinary skill in the art after reading the cited references would have combined the compounds of *Gaillard Kelly* with the compounds of *Partain, Smith*, and *Cremophor*® pamphlet. The Office has failed to show that one of ordinary skill in the art would have had an expectation of success when combining the cited references to obtain a composition as instantly claimed. Regardless of whether the Office's uses an "obvious to try" approach or not, the Office needs to show that one of ordinary skill in the art would have had a reasonable expectation of success when combining the references. M.P.E.P. 2143.02.I (stating that "[t]he prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success.")

In this case, the Office has not met its burden because it has failed to explain how one of ordinary skill in the art would have expected to obtain a successful composition for the delivery of an active compound comprising, *inter alia*, a plasticizer, when no cited reference discloses a compound having such functionality or that the compounds of formula (I) are not among the limited number of compounds that were known to have been soluble in *Cremophor*® RH 40, according to *Cremophor*® pamphlet.

For example, *Smith* teaches that "[t]he therapeutic agents should be chemically compatible with the other ingredients of the composition." *Smith* at col. 4, ll. 47-48.

Also, the instant specification explains that "precipitates of the substances at the application site after evaporation of the solvent" occurred with conventional aqueous/alcoholic hair lotions. Specification at p. 3, line 25 to p. 4, line 5. Therefore, even if the references were combined, the office has not provided any evidence that one of ordinary skill in the art would have expected that the compounds of *Gaillard* would have been chemically compatible with the ingredients of the compositions of *Smith* or *Partain*.

For at least these reasons, the Office has not met its burden of proving a prima facie case of obviousness and Applicants respectfully request that this rejection be withdrawn.

2. **Even if the references are combined, they fail to produce the claimed invention**

Even if one were to accept the Office's rationale for combining the cited art, the combination does not meet all the limitations of the claims. In an effort to expedite prosecution, Applicants have amended independent claims 1, 22, 23, 28, and 29, from which all other claims depend, to recite that "the plasticizer is from 0.05 percent by weight to 2.5 percent by weight" of the claimed composition. Support for the amendment can be found, for example, in the specification at the last full paragraph of page 13 (lines 22-27).

Applicants respectfully point out that the Cremophor[®] pamphlet, the reference the Office is relying on to allegedly provide teachings of POE hydrogenated castor oil's utilization as a plasticizer, fails to provide teachings that would have indicated the claimed range of amounts by percent weight of a composition of a plasticizer. Indeed, the solubility of the retinoids, vitamin A palmitate and vitamin A propionate, are

particularly exemplified by Cremophor[®] pamphlet, which appear to show that the solubility of these retinoids is not attained until the concentration of Cremophor[®] RH 40 is as much as at least 5% in an aqueous solution. See Cremophor[®] pamphlet at 3, ¶ 2, and Fig. 1 and at 4, Fig. 2. As can be seen from the Cremophor[®] pamphlet, vitamin A palmitate and vitamin A propionate are the forms of vitamin A for which the best solubility results are obtained, and, therefore, it would be expected that other retinoids would require an even higher concentration of Cremophor[®] RH 40 to be properly solubilized. See *id.* at ¶ 2. Indeed, an even higher concentration of Cremophor[®] RH 40 is shown to be required to solubilize vitamin E acetate, vitamin D₂, vitamin D₃, and vitamin K, the only other fat-soluble (i.e., hydrophobic) compounds that are exemplified by Cremophor[®] pamphlet. See *id.* at 4, Fig. 3, and at 4, ¶ 1.

In view of these results, it is clear that the teachings in the Cremophor[®] pamphlet would have precluded one of ordinary skill in the art at the time of the invention from having a reasonable expectation of success of a retinoid compound being solubilized in a composition wherein the concentration of POE hydrogenated castor oil is 2.5% by weight or less. As such, the teachings of the cited art cannot be combined based on their alleged teaching of dissolving retinoid compounds in Cremophor[®] RH 40 because the Cremophor[®] pamphlet would have led an ordinarily skilled artisan to conclude that retinoids would not be properly soluble when the amount of plasticizer in a composition does not exceed 2.5%. For at least this reason the Office's burden of creating a case of obviousness has not met the standard required by M.P.E.P. §§ 2142-2145, and emphasized by *KSR Int'l Co. v. TeleFlex Inc.* Accordingly, Applicants respectfully request that the rejection of the instant claims under 35 U.S.C. 103(a) be withdrawn.

3. **The Office's arguments regarding reasons to combine the references do not apply to claim 23**

Claim 23 is an independent claim that is directed to a process for the treatment of androgenic alopecia. The Office's arguments for combining *Gaillard* with *Partain*, *Smith*, and the Cremophor® pamphlet have been focused on the Office's allegation that *Gaillard* teaches that the instant compounds of formula (I) can be combined with retinoids for the treatment of acne. Office Action at 5. According to the Office, the film-forming compositions of *Partain* can also be used to deliver retinoic acid, and the Cremophor® pamphlet teaches that Cremophor® RH 40 is a good solvent for solubilizing retinoic acid. *Id.* The Office concludes that it would have been obvious for one of ordinary skill in the art to have added retinoic acid to the compounds of formula (I) of *Gaillard*, and then use such combination in the compositions of *Partain*. *Id.* The Office further argues that one of ordinary skill in the art would have used Cremophor® RH 40 to solubilize the retinoic acid in those compositions. *Id.*

However, even assuming, *arguendo*, that one of ordinary skill in the art would have combined the references for the purpose suggested by the Office, such combination does not apply to claim 23. Retinoic acid and retinoids in general are useful in the treatment of acne because of their antibiotic properties. *Gaillard* at col. 9, ll. 56-59. Given that claim 23 is directed to the treatment of androgenic alopecia, and that none of the references teaches or suggests the use of antibiotics (or retinoids) for the treatment of alopecia, one of ordinary skill in the art would not have combined the references as suggested by the Office. For this additional purpose, claim 23 is not obvious and Applicants respectfully request that this rejection be withdrawn.

B. Claims 15, 18, 19, 20 and 21

Claims 15, 18, 19, 20, and 21 also remain rejected under 35 U.S.C. 103(a) for reasons of the Record. Office Action at 5. Because claims 15, 18, 19, 20, and 21 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited art, claims 15, 18, 19, 20, and 21 cannot be obvious in light of the cited references either. Accordingly, Applicants respectfully request that the rejection of claims 15, 18, 19, 20, and 21 be withdrawn.

Conclusion

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 1, 2, 4-8, 22, 23, 28, 29 and 40 in condition for allowance. Applicants submit that the proposed amendments of claims 1, 2, 4-8, 22, 23, 28, 29 and 40 do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Furthermore, Applicants respectfully point out that the final action by the Examiner presented some new arguments as to the application of the art against Applicant's invention. It is respectfully submitted that the entering of the Amendment would allow the Applicants to reply to the final rejections and place the application in condition for allowance.

Finally, Applicants submit that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

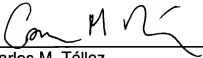
In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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Dated: April 13, 2009

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